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Part II



THE RETENTION AND EXCRETION OF SELENIUM AFTER THE ADMINISTRATION OF SODIUM SELENITE TO WHITE RATS¹

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The metabolism of selenium compounds has within recent years become a problem of increasing importance. The toxicity of the salts of selenium and the wide distribution of this element in the soils and vegetation of certain regions in the Great Plains area has stimulated research concerned with its effects on animals and plants and its mode of action in the living organism. New and more exact methods for the quantitative determination of small amounts of selenium in soils and in biological materials have made possible study of aspects of this problem heretofore impossible.

Since the effects of selenium administered in small amounts over a period of days are cumulative, it has been believed that selenium was retained by the animal organism. Dudley and Byers (1) reported the presence of selenium in the tissues, blood, feces and urine of all animals which had received seleniferous food. In livestock, in which ingestion of sodium selenite had resulted in acute selenium intoxication (2), appreciable amounts of selenium could be detected in blood, bile and urine and in various organs, the concentrations being highest in liver, kidney and spleen. The livers contained from 10 to 25 p.p.m. of selenium. The presence of selenium in the urine and feces of poisoned animals as well as in the urine of workers in the industries utilizing

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selenium (3) suggested, however, that, although the toxic effects of selenium were cumulative, the element itself was rapidly removed from the body. In the tissues of rats fed seleniferous wheat (4), only a small proportion of the ingested selenium was present in the tissues, while a very considerable percentage was excreted in the urine and feces. After the withdrawal of selenium from the diet, the retained selenium was rapidly excreted.

In an attempt to correlate selenium intake, its distribution in the tissues and its elimination (5), varying amounts of sodium selenite were administered either orally or subcutaneously to cats over periods of from 15 to 188 days. A definite relationship between the dosage of selenium administered and its concentration in the urine was established. From 50 to 80 per cent of the total selenium intake was excreted by the kidneys, while amounts ranging from traces to 18 per cent were present in the feces. In chronic selenium intoxication, the element was widely distributed throughout all body tissues. When the administration of the selenium was discontinued, the greater part of the retained selenium was eliminated within two weeks, although small amounts continued to be excreted in the urine and could be demonstrated in the tissues, notably the liver, for as long as a month.

Few of the studies concerned with the elimination or retention of selenium have been carried out with the white rat, an animal which, of the species studied, is most resistant to selenium intoxication (6). Since we had in progress a series of nutritional experiments with white rats in whose diets small amounts of sodium selenite had been incorporated (7), it seemed desirable to determine to what extent selenium was stored in the organs of this species and the relation of factors such as concentration of selenium in the diet or total selenium intake to storage or excretion. It was of interest to determine whether the greater resistance of the rat to selenium intoxication, as compared with other species, could be related to differences in storage or excretion.

Young white rats of approximately 60 gm. weight were maintained on basal diets,² which were deficient in their content of the

² The basal diet (8) contained casein, 6 per cent, starch, 50 per cent, sucrose, 15

sulfur-containing amino acids. These diets were supplemented by cystine or methionine in amounts adequate to promote good growth. Sodium selenite was incorporated into the salt mixture so that the diets as fed contained selenium at levels of 25, 35 and 50 p.p.m. respectively. The daily food consumption of each animal was determined accurately. The addition of the selenium inhibited the growth of the animals markedly. However, since the type of dietary supplement did not appear to influence the retention of the selenium, the details of the growth studies, which are to be presented elsewhere, will not be discussed here.

The feces of the individual animals were collected, carefully separated from any particles of food which might have fallen through the wire mesh of the bottom of the cage and preserved in loosely stoppered flasks until the termination of the experiment.

The selenium-containing diets were fed over periods ranging from 28 to 143 days. At the conclusion of the experiment, the animals were sacrificed and the organs (liver, kidneys, spleen, heart and lungs) were removed and placed in 10 per cent formalin solution.³ The small size of the organs of the young and poorly nourished rats made separate analyses of each organ impossible. Hence, liver, kidneys and spleen (the organs reported to contain the highest selenium concentrations) of each animal were combined and analyzed together. The hearts of 6 rats and the lungs of 4 animals were also analyzed.

The analyses for selenium were carried out by a modification (9) of the method of Horn, which involved digestion of the dry powdered feces or defatted organs (9) with sulfuric acid and mercuric oxide. Aliquots of the digest were allowed to react with codeine sulfate and the intensity of the resulting blue color was measured in a Pulfrich photometer. In a few instances, the method of Robinson, Dudley, Williams and Byers, as modified by Dudley and Byers (1), was used for the analyses of the feces, where larger samples were available for analyses.

per cent, lard, 25 per cent and salt mixture (Osborne-Mendel), 4 per cent. The animals also received the usual supplements of cod liver oil and brewer's yeast fed separately.

³ Experiments cited elsewhere (9) demonstrated that no selenium was extracted from the tissues by the formalin.

The results of the tissue analyses of about 50 individual rats are presented in table 1 and are grouped according to the concentration of selenium in the diet and the relative intakes of selenium throughout the experiment. The concentration of selenium in the combined liver, kidneys and spleen was small and relatively constant, even though the amount of selenium in the diet and the number of days on the diet were variable. In general, more selenium was present in the organs of those rats which had received the toxic diets for longer periods of time.

TABLE 1

Analyses of organs of rats fed experimental diets containing sodium selenite

The values given are the averages obtained for the combined liver, kidneys and spleen of individual rats.

NUMBER OF RATS	Se CONTENT OF DIET	AVERAGE NUMBER DAYS ON DIET	AMOUNT OF Se INGESTED PER RAT		AVERAGE Se CONTENT OF ORGANS
			Range	Average	
	<i>p.p.m.</i>		<i>mgm.</i>	<i>mgm.</i>	<i>mgm.</i>
1	25	91	7-10	9.2	0.09
1	25	91	10-15	11.3	0.08
2	25	143	15-20	17.6	0.08
14	35	37	2-4	3.3	0.06
17	35	49	4-7	5.4	0.08
6	35	57	7-10	8.7	0.10
2	35	67	10-15	11.1	0.11
1	35	112	15-20	17.1	0.14
3	50	38	4-7	4.7	0.05
2	50	59	10-15	11.2	0.07
Hearts from 6 rats	35	57		7.3	None
Lungs from 4 rats	35	55		7.0	0.03

These animals which were able to survive over longer periods of time were also larger and the weight of the organs was greater than that of the animals in which the symptoms of selenium intoxication were manifested early in the experiment. The total selenium in the organs of the individual rats ranged from 0.03 to 0.17 mgm., values which are comparable to those reported (4) for the total internal organs of rats with chronic selenium poisoning (0.06-0.23 mgm.). Small amounts of selenium were present in the lungs and none could be detected in the hearts of 6 rats receiving the selenium diets. The result of this single analysis

of the heart does not agree with the data obtained in cats (5) which indicated a higher content of selenium in the heart than in the lungs. The presence of such minute amounts of the toxicant in the internal organs indicates that true storage had not occurred in these organs; in practically all cases, the amount of selenium found was less than the selenium ingested the day previous to the sacrifice of the animal.

TABLE 2
Analyses of feces of rats fed selenium diets containing sodium selenite

NUMBER OF RATS	Se CONTENT OF DIET	AVERAGE NUMBER DAYS ON DIET	AMOUNT OF Se INGESTED PER RAT		AVERAGE TOTAL Se IN FECES	RECOVERY OF INGESTED Se IN FECES
			Range	Average		
Modified method of Horn						
	<i>p.p.m.</i>		<i>mgm.</i>	<i>mgm.</i>	<i>mgm.</i>	<i>per cent</i>
13	35	37	2-4	3.32	1.05	32
13	35	47	4-7	5.36	1.97	37
2	35	62	7-10	7.93	1.88	24
1	35	74	10-15	11.15	2.75	25
1	35	112	15-20	17.10	9.41	55
2	50	30	2-4	2.99	0.95	32
3	50	38	4-7	4.74	1.41	30
2	50	59	10-15	11.13	4.61	43
Method of Robinson, Dudley, Williams and Byers						
2	25	54	4-7	5.6	3.5	59
2	25	75	7-10	9.0	3.5	38
1	35	56	2-4	3.7	1.2	32
3	35	60	4-7	5.6	2.3	42
2	35	60	7-10	8.9	2.7	30
1	35	60	10-15	11.0	4.7	43

A study of the fecal content of selenium (table 2) showed that no significant correlation existed between the level of dietary selenium and the excretion of selenium in the feces. With few exceptions, from 20 to 50 per cent of the selenium taken in the diet was recovered in the feces. The results obtained by the use of the modified method of Horn (9) and that of Dudley and Byers (1) were similar.

In order to determine whether the fecal selenium represented

metabolic selenium or dietary selenium which had failed of absorption, five rats received sodium selenite parenterally (table 3). Two rats died within 12 hours and 21 to 25 per cent of the selenium injected was present in the combined liver, kidneys and spleen of these animals. The other animals were killed after one week. No selenium could be recovered from the combined organs analyzed. The analyses of the feces of the 3 rats, collected over a period of 7 days after a single injection of selenium, showed that from 2 to 10 per cent of the injected selenium could be demonstrated in the feces. It appears that most of the fecal selenium

TABLE 3

Analyses of organs (combined liver, kidneys and spleen) and feces of rats injected with sodium selenite

Rats 78 and 84 lived approximately 12 hours after the injection; the others were killed at the end of one week.

RAT NUMBER	TOTAL Se INJECTED	MODE OF INJECTION	TOTAL Se IN ORGANS	Se RETAINED IN ORGANS	TOTAL Se IN FECES	RECOVERY OF INJECTED Se IN FECES
	mgm.		mgm.	per cent	mgm.	per cent
78	0.7	Intraperitoneal	0.145	21		
84	0.5	Subcutaneous	0.126	25		
90	0.4	Subcutaneous	0.00	0	0.04	10
92	0.4	Subcutaneous	0.00	0	0.02	5
100	0.5	Intraperitoneal	0.00	0	0.01	2

of rats fed diets containing sodium selenite represents selenium which has failed of absorption from the intestinal tract. Similar results were obtained with cats by Smith, Westfall and Stohlman (5), who recovered 10 to 18 per cent of orally ingested selenium in the feces, while, when the selenium was injected subcutaneously, the selenium content was much less than after oral administration.

In conclusion, it should be emphasized that in the present series, inorganic selenium was administered, i.e., sodium selenite. When natural foodstuffs containing selenium, presumably in organic combination, are fed to rabbits, the selenium appears to be retained to a greater extent than when inorganic selenium compounds were fed (10).

SUMMARY

Young white rats were fed synthetic diets containing sodium selenite at levels of 25, 35 and 50 p.p.m. of selenium. The selenium content of the combined liver, kidneys and spleen of individual rats fed sodium selenite over prolonged periods ranged from 0.03 to 0.17 mgm. or from 0.4 to 2.8 per cent of the selenium ingested. No correlation between the selenium concentration of the diet and that of the organs could be demonstrated. Ingested selenium appeared to be rapidly eliminated by the organism of the rat.

From 20 to 50 per cent of orally ingested selenium was excreted in the feces. No relation between the selenium content of the feces and the concentration of selenium in the diets could be demonstrated. It is believed that the greater part of the fecal selenium originates from dietary selenium which has escaped absorption.

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